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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
JAMES SCOTT CROWE ET AL.

Serial No. 08/378,939

Filed: January 26, 1995

For: PRODUCTION OF ANTIBODIES

Examiner: C. Eisenschenk

Group Art Unit: 1806

RECEIVED

OCT 02 1995

PRELIMINARY AMENDMENT

OCT 03 1995

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to the examination of the above-referenced patent application, Applicants request that the following comments and the contents of the enclosed declaration be considered.

This application is a continuation of application Serial Number 07/952,640. In an Advisory Action issued in connection with the '640 application, the Examiner stated that the Applicants' arguments in favor of patentability were not persuasive because there was no showing that the method claimed produces unobvious results as compared to the prior art. Enclosed herewith is a declaration by Dr. Alan Lewis, one of the inventors of the invention disclosed and claimed in the present application. In the declaration, Dr. Lewis explains in detail why it was not obvious in view of the art cited by the examiner to make recombinant antibodies according to the Applicants' method. The primary reference cited by the Examiner, Gillies et

al., teaches that the light chain of an antibody can be obtained from cDNA encoding both the variable and constant regions of the antibody chain. Gillies et al. teach, however, obtaining the heavy chain of an antibody by expressing a DNA sequence comprising cDNA encoding the variable region linked to genomic DNA encoding the constant region. In his declaration, Dr. Lewis explains that at the time of the present invention it was believed necessary to remove the 3' untranslated region of the DNA sequence encoding each chain of the desired antibody prior to expressing the antibody. For the sequence encoding the light chain of the antibody, a restriction enzyme could be used in a partial digest to remove the 3' untranslated sequence in the constant region DNA. For the constant region of the heavy chain, however, no restriction enzyme recognition sites exist to allow cleavage of the sequence to remove the 3' untranslated sequence. As a result, Gillies et al. grafted genomic DNA encoding the heavy chain constant region to cDNA encoding the variable region of the heavy chain of the antibody of interest. Accordingly, at the time of the present invention, it was believed by those of skill in the art that in order to produce a recombinant antibody it was necessary to remove the 3' untranslated region of the sequence encoding each of the heavy and light chains and that, for the heavy chain, this could only be achieved by removing the sequence encoding the constant region and replacing it with genomic DNA of the appropriate Ig class. The present inventors, in contrast, surprisingly found that the entire cDNA, including

the polyadenylation sequence and preceding untranslated region, was suitable for expression of both heavy and light chains of an antibody.

Applicants respectfully submit that, in view of the statements made by Dr. Lewis in his declaration, the claims of the present application are in condition for allowance. An Notice of Allowance is earnestly solicited.

Respectfully submitted,

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